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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/934,680	08/23/2001	Duncan W. McBranch	8971-017-27	8385

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EXAMINER	
LU, FRANK WEI MIN	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 03/31/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 09/934,680	**Applicant(s)** MCBRANCH ET AL.	
	Examiner Frank W. Lu	**Art Unit** 1634	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 2/24 and 3/1/2005 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The reply was filed after the date of filing a Notice of Appeal, but prior to the date of filing an appeal brief. The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *1-13 and 22-24*.
   Claim(s) withdrawn from consideration: *14-21*.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: see atatched office action .
12. ☒ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). 3/2005
13. ☒ Other: PTO-892.

DETAILED ACTION

Advisory Action

1. The requests for reconsideration filed on February 24, 2005 and March 1, 2005 have been fully considered and entered, and terminal disclaimer filed on February 24, 2005 has been accepted.

Response to Arguments

I. In page 6, first paragraph of applicant's remarks filed on February 24, 2005, applicant argues that the limitation "the fluorescer molecules comprise a plurality of fluorescers pendent on a non-conjugated polymer backbone" recited in claim 23 is not a new matter because the specification (pages 10, lines 5-9 and 21-22, and page 16, lines 17-18 of the specification) supports this limitation.

This argument has been fully considered but it is not persuasive toward the withdrawal of the rejection because the specification (pages 10, lines 5-9 and 21-22, and page 16, lines 17-18 of the specification) only describes that dye polymers that have an ionic fluorescent dye chromophore on each repeat unit on a non-conjugated polymer have previously been shown to exhibit strong J-aggregate absorption and fluorescence (e.g., see the specification, page 10, second paragraph) and does not teach that a plurality of fluorescers is pendent on a non-conjugated polymer backbone. Since an ionic fluorescent dye chromophore can attach to a repeat unit on a non-conjugated polymer by several different ways, for example, an ionic fluorescent dye chromophore can be a part of a repeat unit on a non-conjugated polymer, and the limitation "the fluorescer molecules comprise a plurality of fluorescers pendent on a non-conjugated polymer backbone" recited in claim 23 narrow the scope of the teachings in the

specification, the limitation "the fluorescer molecules comprise a plurality of fluorescers pendent on a non-conjugated polymer backbone" recited in claim 23 is a new matter.

II. In page 6, second paragraph bridging to page 10, second paragraph of applicant' remarks filed on February 24, 2005, applicant argues that Heller does not teach " a conjugated backbone" because "the art recognized definition of conjugated structures such as conjugated polymers is a structure possessing a de-localized pi-electron system (e.g., a structure comprising alternating double and single bonds). See, for example, column 1, lines 21-24 of U.S. Patent No. 6,833,432 B2, a copy of which is attached. Polymers with conjugated backbones are also described in Sandman, 'semiconducting Polymers and their Solid-state Properties', TRIP, Vol. 2, No. 2, February 1994 and Wallace et al., 'conjugated Polymers: New Materials for Photovoltaics', Chemical Innovation, Vol. 30, No. 1, pp. 14-22, April 2000. Copies of these references are submitted herewith. Moreover, the dictionary definition of the term 'conjugated' in the context of organic chemistry is 'relating to or containing a system of two double bonds separated by a single bond' (Websters Third New International Dictionary 1986). See also McMurry, 'organic chemistry', 1984, page 409, a copy of which is also attached" and "it is clear from the context in which the term 'conjugated' is used in the specification that this term is properly defined as 'relating to or containing a system of two double bonds separated by a single bond'. In particular, the specification provides various specific examples of conjugated polymers all of which possess this characteristic alternating single-double bonded backbone structure".

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection. First, there is no definition for "conjugated backbone" in the specification. Second, according to the dictionary, "conjugated" is defined as: (1) "formed by

the union of two compounds; as, a conjugated protein"; (2) "joined together especially in a pair or pairs"; and (3) "containing two or more double bonds each separated from the other by a single bond; -of an organic compound or of the double bonds thus arranged" (see attachment for the definition of "conjugated"). In view of the definition of "conjugated" and the applicant's arguments, it appears that applicant's argument is based on the third definition "conjugated". However, since "conjugated" can also be defined as "formed by the union of two compounds" and the bases of the single DNA polynucleotide strand taught by Heller are connected by 3', 5'-phosphodiester bonds (ie., formed by the union of two bases), Heller teaches a conjugated backbone (ie., the single DNA polynucleotide strand) as recited in the claims.

III. In page 10, four paragraph bridging to page 11, second paragraph of applicant' remarks filed on February 24, 2005, applicant argues: (1) "it is respectfully submitted that the Official Action has failed to establish a *prima facie* case of obviousness since the proposed combination of Heller and Chen would render the complex disclosed by Heller unfit for its intended purpose. In particular, Heller relies upon the hybridization of the polynucleotide strand to which the donor chromophores are attached to achieve the appropriate spacing for efficient donor-donor and donor-acceptor energy transfer (Figure 2A of Heller). The fluorescent polymer of Chen does not have a polynucleotide backbone and would therefore not hybridize to a target nucleic acid. Accordingly, substitution of the MPS-PPV polymer of Chen in the complex of Heller would result in a complex which is unfit for its intended purpose (ie., hybridization to a target resulting in efficient donor-donor and donor-acceptor energy transfer)"; and (2) "the relevant issue is not whether the fluorescent moiety of Chen produces an amplified signal but, rather, whether the proposed substitution would render the complex disclosed by Heller unfit for its intended

purpose. Since the construct disclosed in Heller relies upon hybridization of the fluorescer (i.e, the polynucleotide strand) to a target nucleic acid and since the fluorescent polymer of Chen would not hybridize to a target nucleic acid, the proposed modification would necessarily render the complex disclosed by Heller incapable of by hybridizing and therefore unfit for its intended purpose".

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection. First, applicant's argument "Heller relies upon the hybridization of the polynucleotide strand to which the donor chromophores are attached to achieve the appropriate spacing for efficient donor-donor and donor-acceptor energy transfer" is incorrect because donor-donor and donor-acceptor energy transfer on the polynucleotide strand taught by Heller is not based upon the hybridization to a nucleic acid that is complementary to the polynucleotide strand (see column 6, last paragraph bridging to column 7, first paragraph). Second, although the fluorescent polymer of Chen does not have a polynucleotide backbone and would therefore not hybridize to a target nucleic acid, the rejection is not based on that the polynucleotide strand taught by Heller hybridizes to a nucleic acid that is complementary to the polynucleotide strand. The rejection is based on the motivation from the reference of Chen *et al.*, wherein the fluorescence moiety taught by Chen *et al.*, would lead to a greater than million-fold amplification of the sensitivity to fluorescence quenching relative to that of corresponding small conjugated molecules with similar structure (see Chen *et al.*, page 12287). Third, the target nucleic acid argued by applicant is not a structural part of a chemical moiety recited in claims 1 and 10 and claims 1 and 10 only require that, in the presence of binding of the recognition element to a target nucleic acid, the fluorescence emitted by the fluorescent moiety is

altered from that emitted when binding between the recognition element and the target nucleic acid does not occurred (an ability of a chemical moiety recited in claims 1 and 10). Fourth, applicant does not provide evidence to show why a chemical moiety recited in claim 10 wherein said fluorescent moiety is a J-aggregate of a plurality of fluorescer molecules cannot hybridize to one of its complementary strands.

IV. In page 11, last paragraph bridging to page 12, second paragraph of applicant's remarks filed on February 24, 2005, applicant's argues that: (1) "[H]eller also teaches away from the proposed combination. In particular, Heller relies upon the spacing of the donor-donor pairs at specified distances on the polynucleotide strand (Column 13, Lines 45-59 of Heller). In fact, Heller teaches that close spacing of the donor-donor pairs can reduce energy transfer efficiency. As set forth in the attached declaration, the chromophores in fluorescent polymers such as MPS-PPV have much closer spacings than those disclosed in Heller"; (2) "[I]t is respectfully submitted that Heller's teaching that the close donor-donor spacings which produce amplified superquenching are not desirable would lead one of skill in the art away from substituting a fluorescer which has such spacings (e.g., the fluorescer of Chen) in the complex of Heller"; and (3) "[T]he proposed modification of Heller would also change the principle of operation of the complex disclosed in that reference. In particular, as set forth above, Heller relies upon the hybridization of the fluorescer (i.e., the polynucleotide strand to which fluorescent donors are attached). As set forth above, mere substitution of the fluorescer of Chen in the Heller complex would render the complex unit for its intended purpose (i.e., the resulting complex could not hybridize to a target nucleic acid). In order to produce a functional construct, the proposed combination would require a substantial redesign of the Heller complex as well as a change in

the basic principle under which that complex was designed to operate (i.e., the hybridization of the fluorescer itself)".

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection. First, although applicant declaration filed on July 22, 2004 states that the chromophore in fluorescent polymers such as MPS-PPV have much closer spacings than those disclosed in Heller, the spacing among these MPS-PPV is not related to spacings among donors taught by Heller because, in the rejection on claim 10, the donors taught by Heller (ie., D in Figure 2A) are replaced by MPS-PPV polymers and is not substituted by MPS-PPV monomers. Second, since the donors taught by Heller (ie., D in Figure 2A) are replaced by of MPS-PPV polymers, the superquenching property of MPS-PPV polymer on the chemical moiety recited in claim 10 would not be affected after the modification of donors of Heller. Third, applicant does not provide evidence to show why a chemical moiety comprising multiple MPS-PPV polymers generated by combined the references of Heller and Chen *et al.,* cannot have a superquenching property.

V. In page 6 of applicant's remarks filed on March 1, 2005, applicant argues "polyphenylene ethynylene polymers were referred to as polymers having alternating single and double bonds along the backbone".

The examiner agrees with applicant that polyphenylene ethynylene polymers are polymers having alternating single and double bonds along the backbone. However, since, according to the dictionary, "conjugated" is defined as: (1) "formed by the union of two compounds; as, a conjugated protein"; (2) "joined together especially in a pair or pairs"; and (3) "containing two or more double bonds each separated from the other by a single bond; -of an

organic compound or of the double bonds thus arranged" (see attachment for the definition of "conjugated"), "conjugated" can be interpreted differently from what applicant suggests.

2. The nonstatutory double patenting rejection has been withdrawn in view of the terminal disclaimer filed on February 24, 2005.

3. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is (571)273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (571)272-0746. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (571)272-0745.

Any inquiry of a general nature or relating to the status of this application should be directed to the Chemical Matrix receptionist whose telephone number is (703) 308-0196.

Frank Lu
PSA
March 23, 2005

FRANK LU
PATENT EXAMINER